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Entry 1 of 8

File: USPT

Apr 25, 2000

US-PAT-NO: 6054442

DOCUMENT-IDENTIFIER: US 6054442 A

TITLE: Methods and compositions for modulation and inhibition of telomerase in vitro

DATE-ISSUED: April 25, 2000

**INVENTOR-INFORMATION:**

NAME	CITY	STATE	ZIP CODE	COUNTRY
Chen; Shih-Fong	San Antonio	TX	N/A	N/A
Maine; Ira	San Antonio	TX	N/A	N/A
Kerwin; Sean M.	Round Rock	TX	N/A	N/A
Fletcher; Terace M.	San Antonio	TX	N/A	N/A
Salazar; Miguel	Austin	TX	N/A	N/A
Mamiya; Blain	Austin	TX	N/A	N/A
Windle; Bradford E.	San Antonio	TX	N/A	N/A
Wajima; Makoto	San Antonio	TX	N/A	N/A

US-CL-CURRENT: 514/45; 435/6, 514/46, 514/47, 514/48, 514/49, 514/50, 514/51,  
536/26.26, 536/27.12, 536/27.2, 536/27.8, 536/27.81**ABSTRACT:**

It was found that normal human stem cells produce a regulated non-processive telomerase activity, while cancer cells produce a processive telomerase activity. Nucleotide analogs, such as 7-deaza-2'-deoxyquanosine-5'-triphosphate (7-deaza-dGTP) were found to be substrates for processive telomerase and incorporated into telomeric sequence. The incorporation of this nucleotide subsequently affected the processivity of telomerase, converting processive telomerase to non-processive telomerase. The incorporation of this nucleotide analogs was also found to inhibit formation of G-quartets by telomeric sequence. Other methods for converting cancer processive telomerase to the more benign non-processive telomerase include partially cleaving the telomerase RNA. The nucleoside analogs were found to be capable of a variety of activities including mediating allosteric-like inhibition of telomerase, premature termination and shortening of telomeric DNA, destabilization of telomeric structure and function and eventually cell death. Understanding the mechanisms of telomerase modulation by the 7-deaza-nucleotides has allowed the design of new telomerase inhibitors, modulators and agents for affecting telomere structure and function. These discoveries have application in the treatment of cancer.

21 Claims, 23 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 22

 **2. Document ID: US 6004939 A**

Entry 2 of 8

File: USPT

Dec 21, 1999

TITLE: Methods for modulation and inhibition of telomerase

DATE-ISSUED: December 21, 1999

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Chen; Shih-Fong	San Antonio	TX	N/A	N/A
Maine; Ira	San Antonio	TX	N/A	N/A
Kerwin; Sean M.	Round Rock	TX	N/A	N/A
Fletcher; Terace M.	San Antonio	TX	N/A	N/A
Salazar; Miquel	Austin	TX	N/A	N/A
Mamiya; Blain	Austin	TX	N/A	N/A
Wajima; Makoto	San Antonio	TX	N/A	N/A
Windle; Bradford E.	San Antonio	TX	N/A	N/A

US-CL-CURRENT: 514/43, 514/45, 514/48, 536/23.1, 536/24.5, 536/26.23, 536/26.26,  
 536/26.7, 536/27.8, 536/27.81

## ABSTRACT:

It was found that normal human stem cells produce a regulated non-processive telomerase activity, while cancer cells produce a processive telomerase activity. Nucleotide analogs, such as 7-deaza-2'-deoxyquanosine-5'-triphosphate (7-deaza-dGTP) were found to be substrates for processive telomerase and incorporated into telomeric sequence. The incorporation of this nucleotide subsequently affected the processivity of telomerase, converting processive telomerase to non-processive telomerase. The incorporation of this nucleotide analogs was also found to inhibit formation of G-quartets by telomeric sequence. Other methods for converting cancer processive telomerase to the more benign non-processive telomerase include partially cleaving the telomerase RNA. The nucleoside analogs were found to be capable of a variety of activities including mediating allosteric-like inhibition of telomerase, premature termination and shortening of telomeric DNA, destabilization of telomeric structure and function and eventually cell death. Understanding the mechanisms of telomerase modulation by the 7-deazanucleotides has allowed the design of new telomerase inhibitors, modulators and agents for affecting telomere structure and function. These discoveries have application in the treatment of cancer.

16 Claims, 16 Drawing figures

Exemplary Claim Number: 1,2,3

Number of Drawing Sheets: 9

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 3. Document ID: US 5852188 A

Entry 3 of 8

File: USPT

Dec 22, 1998

TITLE: Oligonucleotides having chiral phosphorus linkages

DATE-ISSUED: December 22, 1998

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Cook; Phillip Dan	Carlsbad	CA	N/A	N/A

US-CL-CURRENT: 536/24.5; 536/25.3, 536/25.33, 536/25.34, 536/25.6, 536/26.1, 536/26.8

## ABSTRACT:

Sequence-specific oligonucleotides are provided having substantially pure chiral Sp phosphorothioate, chiral Rp phosphorothioate, chiral Sp alkylphosphonate, chiral Rp alkylphosphonate, chiral Sp phosphoamidate, chiral Rp phosphoamidate, chiral Sp phosphotriester, and chiral Rp phosphotriester linkages. The novel oligonucleotides are prepared via a stereospecific SN<sub>n</sub>.sub.2 nucleophilic attack of a phosphodiester, phosphorothioate, phosphoramidate, phosphotriester or alkylphosphonate anion on the 3' position of a xylonucleotide. The reaction proceeds via inversion at the 3' position of the xylo reactant species, resulting in the incorporation of phosphodiester, phosphorothioate, phosphoramidate, phosphotriester or alkylphosphonate linked ribofuranosyl sugar moieties into the oligonucleotide.

16 Claims, 0 Drawing figures

Exemplary Claim Number: 1

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 4. Document ID: US 5756291 A

Entry 4 of 8

File: USPT

May 26, 1998

US-PAT-NO: 5756291

DOCUMENT-IDENTIFIER: US 5756291 A

TITLE: Aptamers specific for biomolecules and methods of making

DATE-ISSUED: May 26, 1998

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Griffin; Linda	Atherton	CA	N/A	N/A
Albrecht; Glenn	Redwood City	CA	N/A	N/A
Latham; John	Palo Alto	CA	N/A	N/A
Leung; Lawrence	Hillsborough	CA	N/A	N/A
Vermaas; Eric	Oakland	CA	N/A	N/A
Toole; John J.	Burlingame	CA	N/A	N/A

US-CL-CURRENT: 435/6; 530/413, 536/23.1

## ABSTRACT:

A method for identifying oligomer sequences, optionally comprising modified base, which specifically bind target molecules such as serum proteins, kinins, eicosanoids and extracellular proteins is described. The method is used to generate aptamers that bind to serum Factor X, PDGF, FGF, ICAM, VCAM, E-selectin, thrombin, bradykinin, PGF2 and cell surface molecules. The technique involves complexation of the target molecule with a mixture of oligonucleotides containing random sequences and sequences which serve as primer for PCR under conditions wherein a complex is formed with the specifically binding sequences, but not with the other members of the oligonucleotide mixture. The complex is then separated from uncomplexed oligonucleotides and the complexed members of the oligonucleotide mixture are recovered from the separated complex using the polymerase chain reaction. The recovered oligonucleotides may be sequenced, and successive rounds of selection using complexation, separation, amplification and recovery can be employed. The oligonucleotides can be used for therapeutic and diagnostic purposes and for generating secondary aptamers.

12 Claims, 6 Drawing figures

5. Document ID: US 5705333 A

Entry 5 of 8

File: USPT

Jan 6, 1998

US-PAT-NO: 5705333

DOCUMENT-IDENTIFIER: US 5705333 A

TITLE: Peptide-based nucleic acid mimics (PENAMS)

DATE-ISSUED: January 6, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Shah; Vibhakar J.	San Francisco	CA	N/A	N/A
Kenyon; George L.	San Francisco	CA	N/A	N/A
Kuntz; Irwin D.	Greenbrae	CA	N/A	N/A

US-CL-CURRENT: 435/6; 435/375, 435/377, 436/86, 436/94, 530/300, 530/333, 536/23\_1,  
536/24\_3, 536/24\_31, 536/24\_32, 536/24\_5

ABSTRACT:

The present invention provides novel nucleic acid mimics (termed "PENAMs") comprising a peptidic backbone and nucleotidic sidechains; the sidechains being oriented in such a way that the PENAM is homomorphous to target nucleic acids with which it can effectively hydrogen bond. Homomorphism is achieved by the incorporation of unusual sterochemical centers, including D-chiral centers and quasi-chiral centers, into the peptidic backbone. The PENAMs are useful for targeting nucleic acid sequences in order to modulate their activity in an "antisense" manner. Targeting can also be used to detect, isolate or modify target nucleic acids.

24 Claims, 14 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 14

6. Document ID: US 5594121 A

Entry 6 of 8

File: USPT

Jan 14, 1997

TITLE: Enhanced triple-helix and double-helix formation with oligomers containing modified purines

DATE-ISSUED: January 14, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Froehler; Brian	Belmont	CA	N/A	N/A
Matteucci; Mark	Burlingame	CA	N/A	N/A

US-CL-CURRENT: 536/23\_5; 435/6, 435/91\_1, 536/23\_1, 536/24\_3, 536/24\_5, 536/27\_2, 536/27\_6, 536/27\_81

ABSTRACT:

Novel oligomers are disclosed which have enhanced ability with respect to forming duplexes or triplexes compared with oligomers containing only conventional bases. The oligomers contain 7-deaza-7-substituted purines or related analogs. The oligomers of the invention are capable of (i) forming triplexes with various target sequences such as virus or oncogene sequences by coupling into the major groove of a target DNA duplex at physiological pH or (ii) forming duplexes by binding to single-stranded DNA or to RNA encoded by target genes. The oligomers of the invention can be constructed to have any desired sequence, provided the sequence normally includes one or more bases that is replaced with the analogs of the invention. Compositions of the invention can be used for diagnostic purposes in order to detect viruses or disease conditions.

58 Claims, 29 Drawing figures

Exemplary Claim Number: 1,10

Number of Drawing Sheets: 29

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7. Document ID: US 5521302 A

Entry 7 of 8

File: USPT

May 28, 1996

US-PAT-NO: 5521302

DOCUMENT-IDENTIFIER: US 5521302 A

TITLE: Process for preparing oligonucleotides having chiral phosphorus linkages

DATE-ISSUED: May 28, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Cook; Phillip D.	Carlsbad	CA	N/A	N/A

US-CL-CURRENT: 536/25\_31; 536/25\_3, 536/25\_33

ABSTRACT:

Sequence-specific oligonucleotides are provided having substantially pure chiral Sp phosphorothioate, chiral Rp phosphorothioate, chiral Sp alkylphosphonate, chiral Rp alkylphosphonate, chiral Sp phosphoamidate, chiral Rp phosphoamidate, chiral Sp phosphotriester, and chiral Rp phosphotriester linkages. The novel oligonucleotides are prepared via a stereospecific SN<sub>sub</sub>.2 nucleophilic attack of a phosphodiester, phosphorothioate, phosphoramidate, phosphotriester or alkylphosphonate anion on the 3' position of a xylonucleotide. The reaction proceeds via inversion at the 3' position of the xylo reactant species, resulting in the incorporation of phosphodiester, phosphorothioate, phosphoramidate, phosphotriester or alkylphosphonate linked ribofuranosyl sugar moieties into the oligonucleotide.

12 Claims, 0 Drawing figures

Exemplary Claim Number: 1

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8. Document ID: US 5212295 A

Entry 8 of 8

File: USPT

May 18, 1993

US-PAT-NO: 5212295

DOCUMENT-IDENTIFIER: US 5212295 A

TITLE: Monomers for preparation of oligonucleotides having chiral phosphorus linkages

DATE-ISSUED: May 18, 1993

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Cook; Phillip D.	Carlsbad	CA	N/A	N/A

US-CL-CURRENT: 536/26\_7; 536/25.33, 536/26.8

ABSTRACT:

Sequence-specific oligonucleotides are provided having substantially pure chiral Sp phosphorothioate, chiral Rp phosphorothioate, chiral Sp alkylphosphonate, chiral Rp alkylphosphonate, chiral Sp phosphoamidate, chiral Rp phosphoamidate, chiral Sp phosphotriester, and chiral Rp phosphotriester linkages. The novel oligonucleotides are prepared via a stereospecific SN<sub>n</sub>.sub.2 nucleophilic attack of a phosphodiester, phosphorothioate, phosphoramidate, phosphotriester or alkylphosphonate anion on the 3' position of a xylonucleotide. The reaction proceeds via inversion at the 3' position of the xylo reactant species, resulting in the incorporation of phosphodiester, phosphorothioate, phosphoramidate, phosphotriester or alkylphosphonate linked ribofuranosyl sugar moieties into the oligonucleotide.

9 Claims, 0 Drawing figures

Exemplary Claim Number: 1

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